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Case Report

Pulmonary mucormycosis after heart-kidney transplantation treated with VATS lobectomy: a case report

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Abstract: Pulmonary mucormycosis is a rare pulmonary infection caused by mucorales pathogen. The common inducing factors include diabetes associated with or without ketoacidosis, neutropenia, malignant tumor, chemotherapy, immunosuppressive agents, organ transplantation, anti-rejection treatment, bone marrow and peripheral blood stem cell transplantation, etc. Pulmonary mucormycosis is very dangerous because of the forbidding progression. Previous literature has shown that focal chronic pulmonary lesions or mucorales ball can be treated with lobectomy. Here, we report a case of pulmonary mucormycosis after combined heart and kidney transplantation treated with systemic antifungal therapy and VATS (Video-assisted thoracoscopic surgery) lobectomy and debridement. However, the patient died of phrenic and gastric mucormycosis perforation and subsequent multiple organ failure. Therefore, this case shows the mortality of patients with mucormycosis after multiple organ transplantation can be very high. The timing of surgical treatment combined with other therapies needs to be further studied.

Keywords: Mucormycosis, transplantation, antifungal, VATS, lobectomy, perforation

Introduction

Mucormycosis is a serious pulmonary fungal infection that is rarely seen in the clinic. Mucor can be found in normal people's mouth and nasopharynx. Generally, it is not pathogenic [1,2], but when the body's immune function decreases, it can invade the bronchi and lung and produce acute inflammation, and also brain and organs of the entire body can be involved through the circulation, and the inhalation of spores is also a pathogenetic pathway [3]. Clinical and imaging features of this disease are not specific, while the pathological features are vascular infarction and tissue necrosis [4-6]. Early diagnosis and reasonable treatment are key points to improve the survival rate. Amphotericin B is the first choice of antifungal therapy, and fluconazole can also be used. Amphotericin B and surgical debridement, as well as the treatment of concurrent diseases, nutritional support, correction of electrolyte disorders, and correction of acidosis can reduce the mortality [7]. Limited chronic pulmonary lesions or mucorales ball can be treated by lobectomy together with persistent application of amphotericin B before and after operation [3]. In this case of mucormycosis after heart and kidney transplantation, although surgical resection of the infected pulmonary lobe and thoracic debridement was performed on the basis of systemic internal medication, the patient's infection continued to deteriorate and eventually the patient died of the phrenic and gastric fundus perforation and multiple organ failure.

Case report

A 63-year-old man was admitted for severe coronary atherosclerotic cardiopathy together with renal failure for about ten years. To get the best treatment effect according to the related preoperative examination, doctors of transplant center performed a one-stage sequential heart and kidney transplantation.

The patient was successfully discharged from the ventilator, and the cardiac and renal func-

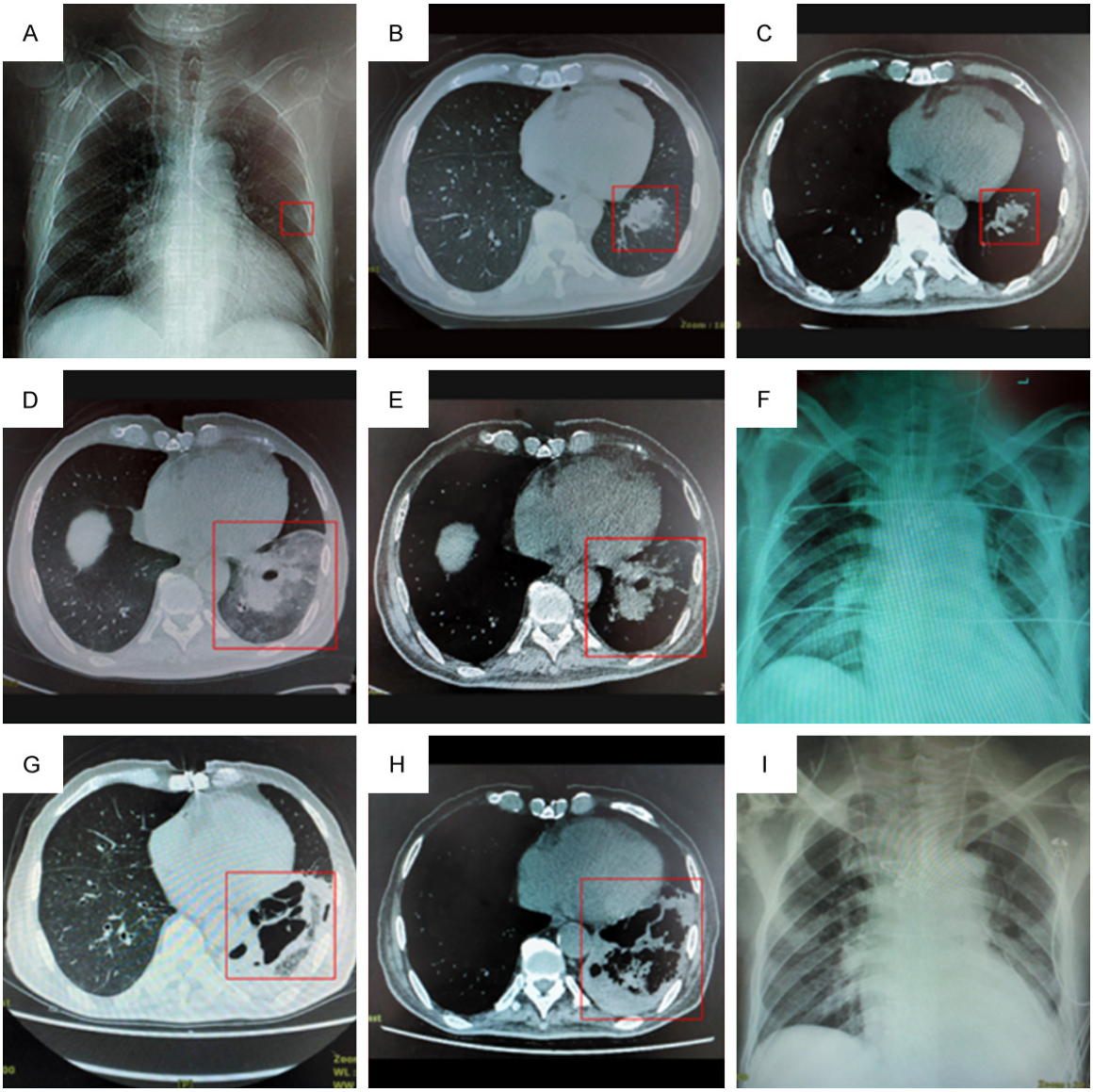

Figure 1. Imaging manifestations of the patient. A. Chest CR on POD 10; B, C. CT scan on POD 10; D, E. CT scan on POD 14; F. CR on the day after the first VATS; G, H. CT scan after perforation; I. CR on the day after the second VATS.

tion recovered well. After the operation, tacrolimus (Tac), mycophenolate mofetil (MMF) and methylprednisolone were given as the immunosuppressive therapy, and piperacillin/tazobactam as an anti-infection medicine. Within one week after operation, the patient's WBC was between 11.38×10^9/L and 16.64×10^9/L, the body temperature fluctuated from 36.9°C to 38.2°C presented an irregular heat type. On the postoperative day (POD) 10, WBC increased constantly to 21.88×10^9/L, chest CR and CT suggested new local focus of infection in the left inferior lung (**Figure 1A-C**). So intensive anti-infective treatment was applied with meropenem and cefoperazone/sulbactam together with voriconazole as antifungal treatment. Sputum culture indicated that ESBL producing Klebsiella pneumoniae infection. Fungal detection of venous blood and sputum was negative. On POD 14, the body temperature rose to 39°C with cough, stale bloody sputum, WBC 19.23×10^9/L, considering the progression of infection, tigecycline was used. Sixteen days after the operation, a chest CT scan showed an infective focus in left lower lobe with the formation of cavity (**Figure 1D**, **1E**). On POD 17, the bron-

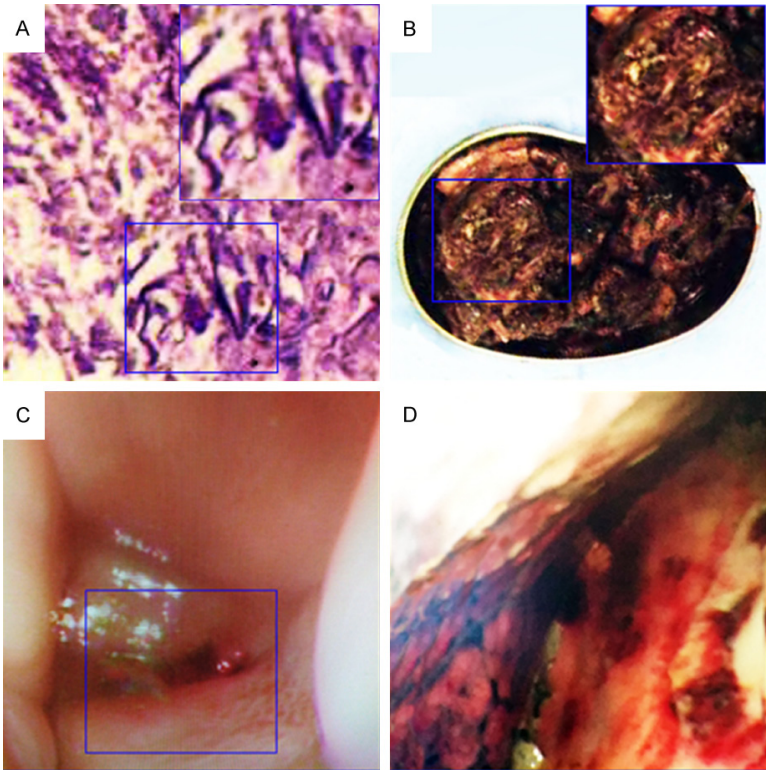

Figure 2. A. Pathology from bronchoscopic biopsy; B. The infected left inferior lobe; C, D. Gastric fundus perforation into the left thoracic cavity from gastroscopy.

choscopy showed that a small amount of bloody purulent secretion in the left basal segment, and the fungal and bacterial culture of the alveolar lavage fluid was retained and tissue was sent for pathological examination. Considering the possibility of G+ cocci infection, Linezolid was used, and the immunosuppressive concentration of Tac and MMF was reduced. On POD 20, pathological exam revealed inflammatory necrosis tissue accompanied by hemorrhage, and mycelium of Mucor could be seen (**Figure 2A**). Intravenous amphotericin B liposome combined with oral paramicrozol was given immediately.

After ten days, a therapeutic session of amphotericin B liposome was given and the infection was gradually localized in the left inferior lobe and also the physical condition improved. After multidisciplinary consultation in the hospital, the patient underwent a VATS left inferior lobectomy, and the suffered lobe was found to have a festering honeycomb shaped area with multiple pus chambers (**Figure 2B**), and the left diaphragm was covered by pus and fibrous plates. After surgery, the left superior lobe inflated well in the thoracic cavity (**Figure 1F**), the thoracic drainage decreased gradually with the amount less than 100 ml, even the fever disappeared within three days. But on the fourth day after lobectomy, shortness of breath, drainage increasing with contents of the stomach were found after nasal feeding. The chest CT scan revealed the presence of hydropneumothorax in the left thoracic cavity (**Figure 1G**, **1H**) and the existence of gastric fundus perforation to the left thoracic cavity was confirmed by gastroscopy (**Figure 2C**, **2D**). Although the endoscopic suture and jejunum nutrition tube placement had been done to perform continuous nutritional support and other comprehensive medical treatment, fever still persisted and even the left hydropneumothorax progressed, therefore, VATS was necessary to debride empyema and close perforation. During the surgery, leakage of the diaphragm and stomach fundus was found infected tissue was removed with an Echelon endocutter. The purulent pneumothorax was relieved (**Figure 1I**) and the contents of the stomach were not drained again, but the patient's general situation deteriorated and eventually died of multiple organ failure.

Discussion

Mucor is a rare and serious conditional pathogenic fungus, most patients are infected by the inhalation of spores in air [2]. Paranasal sinus and lung are the most common sites of infection. The second pathway is transdermal route, skin trauma can make it invade the skin [8]. The presence of high risk factors such as diabetes, malignant tumor, agranulemia, AIDS, malnutrition, application of glucocorticoid or deferoxamine can make mucor to be the third most invasive fungal infection after aspergillus and candida [9]. Although the incidence of mucormycosis is only 8.1%-13%, but the mor-

tality rate is up to 70%-96% [10, 11]. There was less than 1% of mucormycosis after solid organ transplantation, but the mortality rate of infected patients was as high as 80% [12]. Some solid organ transplant recipients develop mucormycosis in the lung with a percentage of about 37%. Most infections occur within 1 year after transplantation [13]. Infected recipients often more than 40 years old and have many risk factors for appeals, especially those with diabetes, application of immunosuppressive agents, patients who often use antifungal agents and uremia [12]. The American Society of Transplantation (AST) has reported that widespread use of antifungal agents such as voriconazole as an independent risk factor for mucormycosis (OR = 10.4), which is even more dangerous than diabetes [14]. Song Yan [13] reported that the mortality of multiple organ transplant recipients complicated by mucormycosis was much higher than that of simple renal transplant recipients (75% and 43.8%). In this case, the patient performed a combined transplantation with advanced age, chronic disease history, malnutrition, routine use of immunosuppressant and large dose of glucocorticoid after operation, unstable blood glucose level and low immunity, so there were many high risk factors, which provide the basis for mucormycosis.

The clinical manifestations of mucormycosis are lack of specificity, fever, cough, dyspnea, and chest pain. The most common symptoms, including hemoptysis can appear after the invasion of blood vessels which is relatively rare but often fatal [15]. Our patient had fever, cough with old bloody sputum. It has been reported that the proportion of dyspnea and hypoxemia in pulmonary mucormycosis is significantly higher than that in general pneumonia. The chest CT scan often shows bilateral lung involvement in a superior lobe, a rapid development into segments, and lobes with multiple thick wall cavities, single or multiple nodules or infiltrating shadows [16]. Our patient's lesion was located in the left inferior lobe as a single infiltrating shadow, which rapidly progressed to the whole left inferior lobe with a thick wall cavity. There is no reliable serological test to confirm the diagnosis of pulmonary mucormycosis. The commonly used G test and GM test can be negative even in the infected patient. Incubation time of lotion pathogen takes a long time, but the positive rate was <5%, while the positive rate of blood culture was much lower. The final diagnosis needs to be built on the discovery of characteristic mycelium in biopsy tissue or positive in aseptic fluid culture [17]. Our patient's symptoms were not typical and the general condition was very poor in the early post operative days, so related invasive examinations were not done in the early stage, such as fiberoptic bronchoscopy, percutaneous lung biopsy, etc., so the early diagnosis was very difficult, although on the 20th day after the operation, the diagnosis was confirmed by bronchoscopic biopsy, but this was somewhat a little late.

The treatment of pulmonary mucormycosis includes removal of risk factors, surgical debridement and early antifungal therapy [18]. As the mucor often invades the blood vessels and causes obstruction, medicine is difficult to play a role in the local lesion, therefore, combined medication with surgery is often used for the treatment of localized lesion. Previous reports show that the mortality of pulmonary mucormycosis treated by medication alone is about 50%-55%, while surgery combined with medication can reduce the mortality to 9.4%-27% [3, 19]. In order to reduce nephrotoxicity, amphotericin B liposome is the first choice for clinical treatment. In the case of amphotericin B invalid, oral polasazol is also effective for some mucormycosis patients [20]. After diagnosis of our patient was clarified, the pulmonary lesion was limited by amphotericin B liposome combined with oral polasazol. After VATS resection of the left inferior lobe, the thoracic condition improved, but because of the strong invasive ability of mucor, diaphragm and gastric fundus infection and perforation lead to the spread. Although the second VATS was performed to close the diaphragm and the fundus and debride the cavity, the infection progressed and the patient eventually died of multiple organ failure. Primary stomach mucormycosis is rare, which often occurs in patients with low immunity and abdominal trauma [21]. It is the first time that mucormycosis causes the perforation of gastric fundus through the diaphragm. Application of immunosuppressive agents and large doses of glucocorticoid resulted in unstable blood glucose level and extremely low immunity in our combined transplant patient, therefore, mucormycosis spread rapidly with strong invasiveness resulting in final death

even though combined with medication and surgical treatment.

In conclusion, the clinical symptoms of pulmonary mucormycosis are complex, and early diagnosis is difficult, so it is easy to misdiagnose. Therefore, patients with high risk factors have rapid progression of pneumonia, especially with ineffective regular antibiotic treatment, irregular thick wall cavity, or halo sign in the chest CT scan, should be considered for mucormycosis. Bronchoscopy, aspiration biopsy, or surgery should then be taken immediately to obtain the pathology. Early diagnosis and early treatment are the key to cure this disease. The basis of the treatment is to remove the risk factors and supportive treatment, once the diagnosis is made, antifungal therapy should be applied as soon as possible, the first choice for medication is amphotericin B, local surgical debridement is also a key point, and combined medication should be done if necessary.

Disclosure of conflict of interest

None.

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